PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 408.86811	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/IB2004/003043	International filing date *(day/month/year)* 28.07.2004	Priority date *(day/month/year)* 28.07.2003
International Patent Classification (IPC) or national classification and IPC A61K31/015, A61K31/136, A61P23/00, A61P29/00		
Applicant MERZ PHARMA GmbH & Co. KGaA		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

   ☒ Box No. I Basis of the opinion
   ☐ Box No. II Priority
   ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   ☐ Box No. IV Lack of unity of invention
   ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   ☐ Box No. VI Certain documents cited
   ☐ Box No. VII Certain defects in the international application
   ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand 28.02.2005	Date of completion of this report 26.08.2005
Name and mailing address of the international preliminary examining authority: European Patent Office - Gitschiner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Authorized Officer Baurand, P Telephone No. +49 30 25901-

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IB2004/003043

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3 and 23.1(b))
   ☐ publication of the international application (under Rule 12.4)
   ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-24 as originally filed

   Claims, Numbers

   1-24 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IB2004/003043

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1 - 24

because:

☒ the said international application, or the said claims Nos. 1 - 24 (with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
☐ has not been furnished
☐ does not comply with the standard

the computer readable form
☐ has not been furnished
☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2 - 5, 11, 12, 15 - 24
	No:	Claims	1, 6 - 10, 13, 14
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1 - 24
Industrial applicability (IA)	Yes:	Claims	-
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item III.

3.1 Claims 1 - 24 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V.

5.1 The following documents are referred to in this communication:

D1: WO 03/040084 A (MERZ PHARMA GMBH &; CO. KGAA; PARSONS, CHRISTOPHER, GRAHAM, RAPHAEL; HE) 15 May 2003 (2003-05-15)

D2: WO 99/01416 A (MERZ + CO. GMBH &; CO) 14 January 1999 (1999-01-14)

D3: WO 01/98253 A (MERZ + CO. GMBH &; CO) 27 December 2001 (2001-12-27)

D4: PARSONS C G ET AL: "Memantine and the amino-alkyl-cyclohexane MRZ 2/579 are moderate affinity uncompetitive NMDA receptor antagonists: In vitro characterisation" AMINO ACIDS, SPRINGER VERLAG, AU, vol. 19, no. 1, 2000, pages 157-166, XP002292645 ISSN: 0939-4451

D5: DANYSZ W ET AL: "AMINO-ALKYL-CYCLOHEXANS AS A NOVEL CLASS OF UNCOMPETITIVE NMDA RECEPTOR ANTAGONISTS" CURRENT PHARMACEUTICAL DESIGN, BENTHAM SCIENCE PUBLISHERS, SCHIPHOL, NL, vol. 10, no. 10, 2002, pages 835-843, XP008030349 ISSN: 1381-6128

5.2 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1, 6 - 10, 13 and 14 is not new in the sense of Article 33(2) PCT.

Document **D1** discloses the same compounds as claimed by the present application and their use for the treatment of chronic and acute pain and migraine (claims 6 and 9).

D2 shows the same compounds as NMDA receptor antagonists and their use for the treatment of chronic and acute pain (claims 1 and 12; page 46, lines 26 and 29).

D3 teaches about the same compounds and their use for the treatment of pain (claims 1, 8 and 9).

D4 reports that a strong evidence exists that MRZ 2/579 (= neramexane) could be useful for the treatment of chronic pain (page 163, last paragraph).

The above documents are therefore considered to be relevant for novelty and inventive step of the subject-matter of claims 1, 6 - 10, 13 and 14.

5.3 Concerning inventive step, the following is pointed out:

The present application differs from the above cited prior art in the condition treated (chronic and acute pain and migraine in D1 - D4 and hyperalgesia, allodynia and neuropathic pain in the present application).

The problem to be solved by the present application may be regarded as providing for compounds useful for the treatment of the above listed conditions.

First, it is considered that the difference between chronic and acute pain and hypersensitivity to pain is very minor. Furthermore, D5 reports that a first Ib phase clinical trial to evaluate the effect of neramexane on hyperalgesia and allodynia has been set up recently (page 842, 5th paragraph). The skilled person would therefore regard the use of 1-amino-alkylcyclohexane derivatives such as neramexane for the treatment of hyperalgesia and allodynia as an obvious option in order to solve the problem posed.

In view of the cited documents, the subject-matter of claims 1 - 24 lacks inventive step (Article 33(3) PCT).

5.4 For the assessment of the present claims 1 - 24 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.